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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,829	12/19/2007	David R. Tabatadze	24028-015 NATL	8389

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Beattie, Ingrid A.
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo
One Financial Center
Boston, MA 02111

EXAMINER	
KETTER, JAMES S	
ART UNIT	PAPER NUMBER
1636	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,829	TABATADZE ET AL.	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *27-40* is/are withdrawn from consideration.

5)☒ Claim(s) *26* is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I, claims 1-26, in the reply filed on 18 November 2010 is acknowledged.

Claims 27-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 18 November 2010.

Claim 26 is allowed.

The disclosure is objected to because of the following informalities:

Some of the Drawings have sequences covered by the Sequence Rules (37 CFR §1.821-1.825). However, these sequences lack the required embedded sequence identifiers (SEQ ID NO….) either in the Drawings or the Brief Description of the drawings in the specification.

Appropriate correction is required.

Claims lack novelty under PCT Article 33(2) as being anticipated by anticipated by Pederson et al.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-19 and 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Pederson et al. (US 5,149,797, newly cited as reference "A").

Claim 1 is drawn to a method for targeted gene repair, comprising contacting a non-repaired target RNA with an RNA oligonucleotide complex comprising a first oligonucleotide and a second oligonucleotide, said first oligonucleotide comprising a sequence complementary to a repaired target RNA, wherein the RNA sequence of the first oligonucleotide comprises an RNase H-resistant modification, and said second oligonucleotide comprises an RNA sequence complementary to at least 6 nucleotides of the first oligonucleotide at the site in the sequence of the first oligonucleotide which is not complementary to the non-repaired target RNA; and hybridizing said complex to said non-repaired target RNA in the presence of an RNase, wherein a repaired RNA is produced. Claim 2 specifies within claim 1 that the repaired target RNA comprises a wild-type sequence. Claim 3 specifies within claim 2 that the non-repaired target RNA comprises a mutation compared to said wild type sequence. Claim 4 specifies within claim 3 that said mutation is a substitution, deletion or insertion of at least one base pair compared to said wild type sequence. Claim 5 specifies within claim 1 that the method further comprises, preceding the steps of claim 1, contacting the non-repaired target RNA with a phosphorothioate (PS) containing sequence comprising a deoxynucleotide with RNase H resistant flanking ends. Claim 7 specifies within claim 1 that said first oligonucleotide is at least 10 nucleotides in length. Claim 8 specifies within claim 7 that said first oligonucleotide comprises about 33 nucleotides. Claim 9 specifies within claim 1 that said second oligonucleotide comprises at least 7 nucleotides. Claim 10 specifies within claim 9 that said second oligonucleotide comprises about 11 nucleotides. Claim 11 specifies within claim 1 that said first oligonucleotide and said

second oligonucleotide are annealed. Claim 12 specifies within claim 1 that contacting said target RNA occurs within a cell. Claim 13 specifies within claim 12 that said cell is in vitro, ex vivo or in vivo. Claim 14 specifies within claim 12 that said cell is a human cell. Claim 15 is drawn to method for treating or ameliorating a symptom of cystic fibrosis in a subject in need thereof, comprising administering an RNA oligonucleotide complex directed to a non-repaired target RNA, said complex comprising a first oligonucleotide and a second oligonucleotide, said first oligonucleotide comprising a sequence complementary to a repaired target RNA, wherein the RNA sequence of the first oligonucleotide comprises an RNase H-resistant modification, and said second oligonucleotide comprises an RNA sequence complementary to at least 6 nucleotides of the first oligonucleotide at the site on the sequence of the first oligonucleotide which is not complementary to the non-repaired target RNA; and wherein administration produces a repaired targeted RNA, thereby treating or ameliorating symptom of cystic fibrosis. Claim16 specifies within claim 15 that the repaired target RNA comprises a wild-type sequence. Claim 17 specifies within claim 16 that the non-repaired target RNA comprises a mutation compared to said wild type sequence. Claim 18 specifies within claim 17 that said mutation is a substitution, deletion or insertion of at least one base pair compared to said wild type sequence. Claim 19 specifies within claim 15 that the method further comprises, preceding the steps of claim 15, administering a phosphorothoiate (PS) containing sequence comprising a deoxynucleotide with RNase H resistant flanking ends. Claim 21 specifies within claim 15 that said first oligonucleotide is at least 10 nucleotides in length. Claim 22 specifies within claim 21 that said first oligonucleotide comprises about 33 nucleotides. Claim 23 specifies within claim 15 that said second oligonucleotide comprises at least 7 nucleotides. Claim 24 specifies within

claim 23 that said second oligonucleotide comprises about 11 nucleotides. Claim 25 specifies within claim 15 that said first oligonucleotide and said second oligonucleotide are annealed.

Pederson et al. teaches a method of site-directed alteration of an RNA molecule using an oligonucleotide that is flanked by nucleotide sequences unable to activate RNase H and a second oligonucleotide that is unmodified and hybridized to the modified oligonucleotides and altering the RNA in the presence of RNase. Furthermore, the alteration can be excision or excision and addition of nucleotides, the oligonucleotides can be modified with phosphorothioates, the flanking sequences can be modified with methyl phosphonates. The method may be used to correct defects in an individual suffering from cystic fibrosis (e.g., at the Abstract, column 1, lines 59-67, columns 2-6 or columns 11-12).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pederson et al. (cited above) in view of Kole et al. (US 5,627,274, newly cited as reference "B").

Claims 1 and 15 are described above, and are included in the present rejection as they encompass all that is claimed by claims 6 and 20, respectively. Claim 6 specifies within claim 1 that said RNase H-resistant modification is the addition of a 2-O-methyl moiety. Claim 20 specifies within claim 15 that said RNase H-resistant modification is the addition of a 2-O-methyl moiety.

Pederson et al. is described above. Pederson et al does not specifically teach modifying the oligonucleotide by adding a 2-O-methyl moiety. Kole et al teaches modifying oligonucleotides with a 2-O-methyl moiety for alteration of RNA molecules (e.g., at column 7, lines 44-67 and column 8, lines 1-7 and 41-56. Column 8, lines 41-55 teach the advantage of 2-O-methyl modified oligonucleotides as being RNase H resistant).

The substitution of one known element (2-O-methyl moieties on oligonucleotides as shown in Kole et al.) for another (the oligonucleotides with the unmodified or unspecified 2 position taught by Pederson et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the 2-O-methyl would have yielded predictable results, namely, (improved) RNase H resistance of the oligonucleotide in the method taught by Pederson et al. Such improved RNase H resistance also would have served as a motivation to one of ordinary skill in the art to employ 2-O-methyl modification of the oligonucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James S. Ketter whose telephone number is 571-272-0770. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSK
28 January 2011

/James S. Ketter/
Primary Examiner, Art Unit 1636